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**TRABALHO FINAL**
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Clínica Universitária de Ortopedia

# Open Vs arthroscopic surgery for diffuse tenosynovial giant cell tumors of the knee: A systematic review

Maria Beatriz Alexandre Quaresma

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**Orientado por:**

Joaquim Soares do Brito

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**Serviço de Ortopedia e Traumatologia do Centro Hospitalar Lisboa Norte-Hospital Universitário de Santa Maria**

**Clínica Universitária de Ortopedia e Traumatologia da Faculdade de Medicina da Universidade de Lisboa**

**Aluna: Maria Beatriz Alexandre Quaresma**

**Orientador: Dr. Joaquim Soares do Brito**

**Clínica Universitária de Ortopedia: Professor Doutor Jacinto Monteiro**


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## Resumo

### Introdução

O tumor tenossinovial de células gigantes (TTCG), mais comummente conhecido por sinovite vilonodular pigmentada, corresponde a uma proliferação benigna da membrana sinovial das articulações, bainhas tendinosas, bursas ou tecido fibroso adjacente a estas estruturas anatómicas. Esta condição pode ser subsequentemente dividida em dois subgrupos, dependendo do seu padrão de apresentação: tumor tenossinovial de células gigantes localizado/nodular (TTCG-L) com um ou mais nódulos infiltrativos da sinovial (mas com padrão morfológico bem definido); ou difuso (TTCG-D), afectando a membrana sinovial de forma multinodular ou como indica o próprio nome, estendendo-se difusamente, sendo difícil estabelecer os limites da lesão. A sua etiologia e patogénese mantêm-se em aberto, podendo estar relacionados com um processo neoplásico benigno, episódios de trauma, cirurgia ortopédica ou alterações do metabolismo lipídico.

A TTCG-L apresenta uma incidência superior à TTCG-D, com 10.2 e 4.1 casos por milhão de habitantes/ano respectivamente, sendo esta entidade mais frequentemente observada em adultos com idades compreendidas entre os 30 e 50 anos, e com uma ligeira predominância no género feminino (1:1.5). A forma difusa da doença caracteriza-se por um crescimento mais rápido e agressivo, com frequente extensão para além da membrana sinovial a estruturas subjacentes, com margens mal delimitadas, pelo que morbilidade associada a este padrão é evidentemente superior, mesmo após tratamento adequado. Tendo em conta as suas dimensões habituais, o padrão localizado apresenta um prognóstico mais favorável, com uma taxa de recidiva  local que oscila entre os 0 e 6%. A presença de doença residual ou a recidiva, com necessidade adicional de cirurgias subsequentes, representa um risco acrescido para a destruição articular, assim como das suas estruturas envolventes. Em última análise poderá ser necessário recorrer a uma artroplastia com o objectivo de melhorar a função e diminuir a morbilidade associada à doença.

A sintomatologia depende da articulação afetada, mas frequentemente manifesta-se por dor, derrame articular de repetição, rigidez articular com limitação da cinética articular, bloqueio e instabilidade. A título global, a articulação do joelho é aquela mais frequentemente afetada, respondendo por cerca de 46% dos TTCG-L e 75% dos TTCG-D.

Dada a baixa incidência e prevalência associadas com os TTCG, a imensa variedade de articulações envolvidas e os diferentes padrões da doença, é difícil estabelecer um tratamento *standard*. O tratamento habitualmente preconizado para abordar um TTCG passa pela sinovectomia cirúrgica, contudo, no caso particular do TTCG-D não é absolutamente consensual a melhor abordagem: via artroscópica ou via aberta/clássica.

**Objetivo**

Com este trabalho, os autores pretenderam promover uma revisão sistemática da literatura, recorrendo a estudos publicados na língua inglesa, no período mediado entre o ano de 2009 a Abril de 2019, de modo a comparar os resultados obtidos com diferentes modalidades cirúrgicas no tratamento TTCG-D no joelho. O objetivo final da revisão sistemática passa por inferir sobre qual a modalidade cirúrgica (artroscópica ou aberta) que permite obter resultados superiores, tendo como critérios de estudo: a taxa de recidiva, a progressão para osteoartrose, a necessidade em realizar uma artroplastia total de joelho, presença de edema, infeções ou deiscência da ferida operatória, dor e limitação da cinética articular.

**Metodologia**

A revisão sistemática foi desenvolvida utilizando como palavras-chave: *"Tenosynovial giant cell tumor [MeSH], OR pigmented villonodular synovitis [MeSH]" AND "surgery" OR "arthroscopic surgery" OR "outcome"* em duas bases de dados electrónicas: Pubmed/Medline e B-on.

Para a revisão sistemática foram considerados todos os estudos observacionais (prospectivos e retrospectivos), caso-controlo, coorte, e ensaios clínicos randomizados encontrados. Os critérios de exclusão estabelecidos previamente incluiram: artigos de revisão ou de *case report*, artigos apenas com abstract disponível e artigos não acessíveis para análise integral. Foram igualmente definidos como critérios de inclusão: população adulta (+ 18 anos), com diagnóstico de TTCG-D do joelho, submetidos a intervenção cirúrgica para tratamento (ora por via artroscópica ou via aberta/clássica), em que fossem explicitados os resultados obtidos com o tratamento realizado.

Foram estabelecidos como *outcomes* primários: a taxa de recidiva, progressão para osteoartrose e a necessidade em realizar uma artroplastia total de joelho; foram definidos como *outcomes* secundários: a presença de edema persistente, dor, limitação da cinética

articular e complicações inerentes à realização de um procedimento cirúrgico, nomeadamente infecção e descendência da ferida operatória.

**Resultados**

Um total de 302 artigos foram inicialmente selecionados tendo em consideração título e *abstract*, dos quais foram excluídos os artigos duplicados e os que não preencheram critérios para inclusão. Foram finalmente selecionados 19 artigos para leitura integral, tendo resultado desta segunda análise uma nova seleção de oito artigos, que foram incluídos na revisão final.

1. ***Outcomes* primários**

***a) Recidiva local***

Da revisão realizada constatou-se que são vários os autores (*Jabalameli et al, Sharma et al.* e *Patel et al.*) que favorecem a sinovectomia aberta em relação à artroscopia, associando a esta técnica uma maior probabilidade de excisão total da lesão primária. Contudo, *Xie Guo-ping et al.,* não constataram diferenças estatisticamente significativas entre as duas metodologias cirúrgicas, sugerindo que existem taxas de recidiva sobreponíveis após sinovectomia aberta ou artroscópica.

Também num estudo não comparativo, *Auregan et al.* e *Jain et al.* observaram taxas de recidiva comparáveis às descritas com técnica aberta, após sinovectomia artroscópica. *Akinci et al.,* contrariamente, observaram superioridade na técnica por via aberta. Simultaneamente, *Colman et al.* verificaram uma menor probabilidade de recidiva após cirurgia faseada (via aberta para uma abordagem posterior e artroscópica para uma abordagem anterior), recomendando uma nova estratégia na abordagem cirúrgica do TTCG-D no joelho.

***b) Osteoartrose e necessidade de artroplastia do joelho***

*Colman et al.* especificaram existir uma menor progressão para osteoartrose nos casos pós-sinovectomia por via aberta, quando comparados com técnica artroscópica, no entanto, não foi possível encontrar diferenças estatisticamente significativas relativamente a este aspecto. *Jabalameli et al.* referem terem registado quatro casos de osteoartrose, enquanto que no grupo de *Akinci et al.* sete doentes foram sujeitos a artroplastia total do joelho após terem

sido submetidos a sinovectomia por via aberta. *Jitesh K et al.* não observaram durante o seu follow-up progressão para osteoartrose ou necessidade de artroplastia total do joelho em nenhum dos doentes em estudo.

**2. *Outcomes* secundários**

***a) Edema, Dor* e *Cinética Articular***

Na avaliação destes parâmetros para a sinovectomia por via aberta, *Akinci et al.* obtiveram no Knee Society Score resultados muito bons e bons em cerca de 42.2% e 47.3% dos doentes, respectivamente. Da mesma forma, em seis doentes *Jabalameli et al.* observaram uma melhoria significativa considerando a mesma escala. *Aurégan et al*. utilizaram outra avaliação funcional, o Tegner-Lysholm score, com significativas melhorias, de 68±10 (pré-operatório) para 90±8 (pós-operatório) em doentes sujeitos apenas a sinovectomia artroscópica. *Patel et al*. e *Akinci et al.* observaram rigidez articular em 1% e 20% dos doentes respectivamente, depois de sinovectomia por via aberta.

***b) Complicações associadas com o procedimento cirúrgicas***

Para os doentes sujeitos a sinovectomia por artroscopia, *Aurégan et al*. e *Jitesh K et al.* reportaram taxas de complicação próximas de 0%. Do mesmo modo, *Jabalameli et al.* não observaram infeções ou lesões neurovasculares com qualquer das técnicas implementadas (artroscópica ou aberta). Por outro lado, *Patel et al.* registam uma taxa global de complicações pós-cirúrgicas por via aberta de 88.9%, enquanto *Colman et al*. verificaram uma taxa de complicação menor no grupo em que foi realizada sinovectomia anterior por via artroscópica e posterior por via aberta (sinovectomia faseada).

**Discussão**

A sinovectomia por via aberta aparenta obter taxas de recidiva inferiores no tratamento do TTCG-D quando comparadas com sinovectomia artroscópica. Dada a característica extensão do TTCG-D para os tecidos e estruturas adjacentes, a recidiva local será maioritariamente influenciada pela doença residual em consequência de uma excisão subtotal. Por essa razão são vários os autores que favorecem a sinovectomia aberta, dado que a via artroscópica parece representar uma probabilidade superior de excisão incompleta da lesão. Devemos, no

entanto, enfatizar o viés existente na avaliação da recidiva local nos estudos incluídos, em grande medida pela ausência de uma definição concreta para análise do fenómeno. É por isso possível e provável, que existam recidivas locais subestimadas pela não valorização das mesmas ou sobre-estimadas, ao considerarem como recidivas locais o remanescente de reseções subtotais da lesão inicial.

A revisão sistemática realizada não permite concluir categoricamente qual a influência da escolha da modalidade cirúrgica para a progressão no sentido da osteoartrose e da necessidade de artroplastia total do joelho, contudo, estes *outcomes* tendem uma vez mais a ser favoráveis ao procedimento cirúrgico por via aberta. É, contudo, necessário realçar a falta de critérios objetivos para o diagnóstico de osteoartrose, assim como dos critérios claros que motivaram a realização de uma artroplastia total do joelho na sequência de um TTCG-D tratado cirurgicamente. Este facto introduz novas variáveis que impedem a obtenção de resultados consistentes, capazes de orientar a atuação clínica.

Analisando os *outcomes* secundários, a sinovectomia por via aberta apresenta comparativamente, uma maior associação com a limitação da cinética articular do joelho, assim como de rigidez pós-operatória. A técnica artroscópica demonstrou ainda superioridade no que se refere à morbilidade e complicações diretamente associadas com a intervenção cirúrgica. No entanto, uma vez mais se destaca a falta de rigor existente na medição destes *outcomes*, assim como a utilização de escalas de avaliação clínica diferentes de estudo para estudo, facto que dificulta a leitura dos resultados, assim como a obtenção de consensos.

No seu conjunto, não poderemos deixar de enfatizar as grandes limitações inerentes a esta revisão sistemática, sendo consequência direta do número e qualidade dos estudos selecionados, facto que traduz a raridade da doença e inerentes dificuldades no seu diagnóstico e tratamento. Será por isso fundamental desenvolver estudos prospectivos multicêntricos, capazes de envolver números significativos de doentes, de modo a permitir obter melhores respostas para as perguntas aqui colocadas. Deste modo e considerando todas as dificuldades associadas ao tratamento do TTCG-D do joelho, assim como as complicações registadas nos artigos incluídos nesta revisão, é pertinente manter a atual pesquisa e desenvolvimento de novas modalidades terapêuticas. Os grandes objetivos desta estratégia passa por minimizar as taxas de recidiva local, melhorar a sobrevida livre de doença, diminuir o potencial para destruição articular e construir uma alternativa válida às terapêuticas cirúrgicas (mais invasivas e tendencialmente dispendiosas). A exploração de

terapêuticas-alvo parece ser a nova tendência, estando a decorrer ensaios clínicos que poderão num futuro próximo trazer novidades para o tratamento desta condição clínica.

**O Trabalho Final exprime a opinião do autor e não da FML**

## Abstract

**Background:** Knee diffuse-type tenosynovial giant cell tumor (D-TGCT) have a very high complication rate. Standard of care for this disease usually involves early surgery with synovectomy, and available surgical techniques include arthroscopic or open surgery, however, there is lacking consensus in which technique and when should be used.

**Purpose:** Compare open and arthroscopic synovectomy outcomes for knee D-TGCT.

**Methods:** We conducted a systematic review for studies published in english language between 2009 and April 2019, using the Pubmed/Medline and B-on electronic databases, to evaluate outcomes after arthroscopic or open synovectomy for knee D-TGCT.
The search terms used were: "Tenosynovial giant cell tumor [MeSH], OR pigmented villonodular synovitis [MeSH]" AND "surgery" OR "arthroscopic surgery" OR "outcome".

**Results:** We analysed 302 articles according with title and abstract and 19 were pre-selected for full reading and analysis. A total of eight assays matching the inclusion criteria were selected: two prospective and six retrospective studies. Recurrence rate for each surgical technique, progression to osteoarthritis and total knee arthroplasty (TKA); wound infection, articular effusion, pain, range of motion and complications directly related with the surgical procedure were extracted.

**Conclusion:** In knee D-TGCT arthroscopic excision is effective to minimize morbidity and surgery related complications, while open surgical techniques showed superiority concerning local recurrence, once it seems to provide a more a successful resection. However, we could not conclude with significant value which of the surgical techniques is better regarding progression towards osteoarthritis and need for TKA.

**Study design:** Systematic review of literature.



**Keywords:** Tenosynovial giant cell tumor; Pigmented villonodular synovitis; Knee; Surgical treatment; Outcome.

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## Introduction

Tenosynovial giant cell tumor (TGCT), prior known as giant cell tumour of the tendon sheath or pigmented villonodular synovitis (PVNS), can also be named xanthogranuloma, benign synovioma and fibrous xanthoma of synovium.[1] The term, finally redefined in the 2013 World Health Organisation classification for bone and soft tissue tumours, refers to a group of rare, benign, inflammatory and proliferative neoplasmatic monoarticular diseases, arising from the tendon sheath, bursae, synovium of the joint or fibrous tissue adjacent to the tendon.[2]

This condition is subdivided in two different subtypes depending on the presentation: local (L), with a single nodule infiltrating the tendon sheath, or diffuse (D), which affects the synovium of a joint surface with multiple nodules or in an absolutely diffuse fashion. [3] This disease is most frequently seen in adults between 30 and 50 years of age, with a slight predominance among females (1:1.5), and a very low incidence: 10.2 per million/year for L-TGCT and 4.1 per million/year in D-TGCT type. [2][4]

Patients with TGCT more commonly presents nonspecific symptoms as pain, repeated non-traumatic joint effusion, stiffness, decreased range of motion, locking and joint instability.[5] Furthermore, D-TGCT is classically found in large joints such as the knee or other weight bearing joints such as the hip, ankles, shoulders and elbows, with a more aggressive growth. On the other hand, L-TGCT usually involves the hands or feet, presenting a better prognosis.[6] The knee joint is the most commonly involved articulation, representing 46% in the localized type and up to 75% in diffuse-type. [7] However, we must stress that any joint can be affected and patients are frequently misdiagnosed as rheumatologic diseases, bleeding disorders or septic arthritis. [5]

Given the low incidence of these particular tumors, variety of joints involved and different biological behaviour, is difficult to establish an absolute standard treatment.[8] The most consensual current choice to treat a diffuse tenosynovial giant cell tumour of the knee is a surgical resection of the lesional tissue, but there is no consensus about the most appropriate type of surgery: either arthroscopic or with an open synovectomy. [9]

The presence of recurrent or residual disease, needing subsequent surgical interventions can be locally devastating to the joint as well as to other surrounding structures as the underlying bone, muscle, neurovascular structures or skin. The sequelae can result in end-stage

degenerative joint disease (DJD), which can indicate the need for total joint arthroplasty, in order to relieve pain and improve function, with higher morbidity and loss of quality of life.[8][9][10][11]

Having this in consideration, the authors looked into the literature and a systematic review regarding the reported outcomes obtained with open and arthroscopic treatment in D-TGCT is herein presented.

## Methods

This study is a systematic comparative review of previously published studies in the english literature, concerning the outcomes regarding open and arthroscopic surgery to surgically treat D-TGCT of the knee. There were used two electronic databases: **Medline/Pubmed and B-on databases,** searching from 2009 to April 2019. We systematically searched for studies that included the keywords/Mesh words: "Tenosynovial giant cell tumor [MeSH], OR pigmented villonodular synovitis [MeSH]" AND "surgery" OR "arthroscopic surgery" OR "outcome". The last date of search was April 7, 2019.

For the inclusion criteria, we applied the Population, Intervention, Comparison, Outcome and Study strategy. We defined:

1. Population- adult population (+18 years) with D-TGCT/PVNS of the knee;
2. Intervention- open surgery which we compared with arthroscopic surgery
3. Outcomes:
    a. **Primary outcomes:**
        i. Recurrence of disease
        ii. Osteoartrosis
        iii. The need for knee arthroplasty
    b. **Secondary outcomes:**
        i. Articular effusion
        ii. Pain
        iii. Limited range of motion
        iv. Complications due to surgery: infeccion or wound dehiscence

4. For this type of study, we included prospective and retrospective observational studies, randomized controlled trials, case-controlled studies and cohort studies.

For the exclusion criteria we considered as follow: review articles and case report studies; articles only with abstract available and articles where the full text was not accessible.

## Results

### *Selected studies*

A total of 302 articles (255 from **Pubmed/Medline** and 47 from **B-on databases)** were initially examined by title and abstract (Fig.1). The selection of the articles followed a rigorous analysis and confirmation of the Mesh keywords searched, the inclusion and exclusion criteria. After excluding the overlap articles between both databases, were pre-selected 19 articles that fulfilled the previously defined criteria (Fig.1). After an integral reading of the pre-selected articles we excluded 11 articles due to lack of clarity and rigor, limited or unclear information considering the outcomes in analysis, the subgroup of disease, treatment for group or specific recurrence within surgical technique (Fig.1). In the final selection we included eight articles, presented in Table 1: two prospective and six retrospective studies.

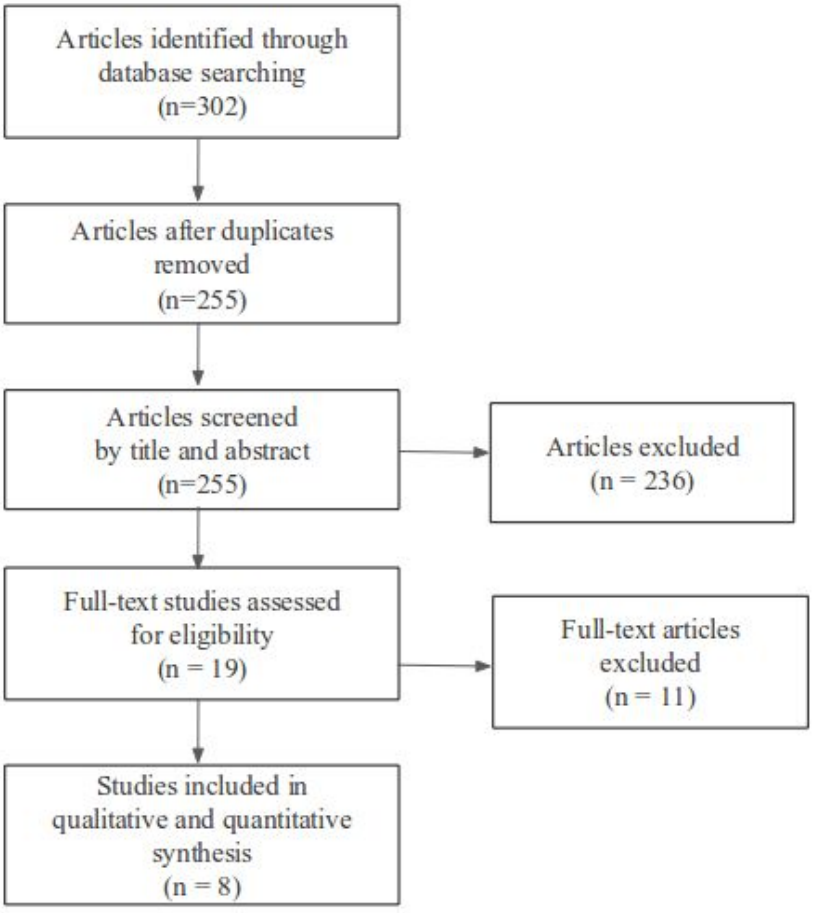


**Fig.1.** Flowchart illustrating the search strategy and number of records screened and included

**Table 1.** Characteristics of the studies included and summary of the results

| Author | Year | Type of study | Number of patients | Average follow-up (months) | Age (median years) | Technique | Recurrence rate | Osteoarthrosis | TKA | Secondary outcomes (patients) |
|---|---|---|---|---|---|---|---|---|---|---|
| Akinci et al. (12) | 2011 | prospective | 15 | 80.2 | 42.8 | open synovectomy | 26,31% | NR | 39% | Stiffness (3), KSS perfect (8 - 42.2%) good (9 - 47.3%) bad (2- 10.5%) |
| Guo-ping et al.(13) | 2015 | retrospective | 175 | 108 | 35.70±16.12 | open synovectomy 57 | 16/57 = 28% | NR | NR | NR |
| | | | | | | arthroscopic synovectomy (118 patients) | 26/118 = 22% | | | |
| Jabalameli, et al.(14) | 2014 | prospective | 15 | 55.2 | 28.2±12.37 | 1 arthroscopic anterior and open posterior synovectomy | 1/1 recurrence | Moderate to severe (2), Bone erosions 33% - 56% | 7% NR to which treatment | KSS 63.1± 6.68 pre operation, 77.8± 9.29 pos operation |
| | | | | | | 7 staged posterior and anterior open synovectomy | 0% | | | |
| | | | | | | 2 all arthroscopic synovectomy | 50% | | | |
| | | | | | | 1 subtotal arthroscopy synovectomy | 0% | | | |
| | | | | | | 4 subtotal open synovectomy | 0% | | | |
| Aurégan et al.,(15) | 2013 | retrospective | 7 | 84 | 41 | Arthroscopic total synovectomy | 29% | NR | NR | Haemarthrosis (1), Tegner-Lysholm score: 68 ± 10 to 90 ± 8, Ogilvie-Harris score: 11 ± 1 |
| Jitesh et al.(16) | 2013 | retrospective | 29 | - | 44 | Arthroscopic synovectomy | 57% (12 patients) | NR | NR | NR |

**Table 1:** (Continued) Characteristics of the studies included and summary of the results

| Author | Year | Type of study | Number of patients | Average follow-up (months) | Age (median years) | Technique | Recurrence rate | Osteoarthrosis | TKA | Secondary outcomes (patients) |
|---|---|---|---|---|---|---|---|---|---|---|
| Colmanet al.(17) | 2012 | retrospective | 48 | 40 | NR | 11 open posterior + open anterior synovectomy | 64% | 0% | 0% | Wound infection (9%) |
| | | | | | | 11 open posterior synovectomy + anterior arthroscopic synovectomy | 9% | 9% | 0% | Hemarthrosis (9%), Stiffness (9 %) |
| | | | | | | 26 all-arthroscopic synovectomy | 62% | 23% | 15% | Hemarthrosis (8%) , DVT (4%) |
| Vivek, et al.(18) | 2009 | retrospective | 37 | 74.4 | 35.2 (10–73) | 16 open/open | 19% | NR | NR | NR |
| | | | | | | 8 anterior arthroscopic synovectomy/open posterior synovectomy | 25% | | | |
| | | | | | | 13 all arthroscopic subtotal synovectomy | 92% | | | |
| Patel et at.(19) | 2017 | retrospective | 102 | 25 | 39 | 84 Open synovectomy | 44.80% | NR | NR | Wound infection (6), Haemarthrosis (3), Stiffness (2), DVT (1) |
| | | | | | | 4 Arthroscopic/Open synovectomy | | | | |
| | | | | | | 12 arthroscopy synovectomy | 83,3% | | | |

DVT = deep venous thrombosis, KSS= Knee Society Score, NR= non reported, TKA= total knee arthroplasty

***Primary Outcomes***

***a) Local recurrence***

*Akinci et al.* observed in a prospective study a subgroup of 15 patients with diffuse tenosynovial giant cell tumor (D-TGCT) of the knee treated with open synovectomy, a recurrence rate of 26% (five subjects). They considered open total synovectomy still a gold standard surgery even though this conclusion is skewed by the sample. [12]

The authors *Guo-ping et al.* analysed a subgroup of 175 cases of D-TGCT in the knee were the patients were either treated with arthroscopic synovectomy (118 cases) or open resection (57 cases) with a global recurrence rate of 24%. They did not identify significant recurrence difference between patients that were treated with open versus arthroscopic surgery ($p = 0.78$) and pointed as limitation for their study the size of the sample, the nature of the study with no case-control and the recurrence rate being only calculated by electronic medical records. [13]

In other comparative (open versus arthroscopic surgery) prospective study, *Jabalameli et al.* involved 15 subjects with D-TGCT with a mean age of 28 years and followed for four and a half years. Five patients underwent subtotal synovectomy – four in the arthroscopic arm and one in the open synovectomy arm. The other 10 cases were divided as follows: two total arthroscopic synovectomies, seven staged posterior and anterior open synovectomies and one arthroscopic anterior and open posterior synovectomy. They observed two cases of recurrence (7%), one with arthroscopic and open synovectomy and other with total arthroscopic technique. Therefore and with this data they concluded that the treatment of choice for D-TGCT should be staged open posterior total synovectomy followed with open anterior synovectomy.[14]

*Aurégan et al*., promoted a prospective study, which involved a subgroup of seven patients with D-TGCT, with a mean age of 41 years, all managed with arthroscopic synovectomy. They were able to follow the group over seven years, during which two patients had a recurrence of the disease, indicating a recurrence rate of 29%. The authors assume that arthroscopic synovectomy enables an effective excision of the primary lesion with a good function, low complication rates and satisfactory disease control, stressing that this first arthroscopic approach would allow a secondary management with open synovectomy in case of recurrence.[15]

*Jitesh K et al.* analysed in a retrospective study a subgroup of 29 cases, with a mean age of 44 years during a mean follow up of seven years. In this group a total arthroscopic excision was performed, and the authors reported a five year recurrence-free survival rate of 57%. 12 patients developed recurrences between three months and two years post operatively. However, no recurrence was noted after two years. The authors concluded that this technique provides such a good result as open synovectomy, but with lower morbidity. [16]

*Colman et al*. retrospectively studied 103 cases where 48 D-TGCT of the knee were treated with: total-arthroscopic surgery, open posterior and anterior arthroscopic synovectomy, open anterior and open posterior synovectomy, or totally open synovectomy. The overall recurrence rate was 50% within a median time of 27 months. They observed a lower recurrence rate in the open posterior with anterior arthroscopic synovectomy group, when compared with the totally arthroscopic or open surgery groups: 9% versus 62% versus 64% - (p=0.008). However, this study has the limitation of the number of patients, with only 11 patients in the group where an open posterior plus anterior arthroscopic synovectomy was performed. [17]

In other study, *Vivek et al.* reached a similar conclusion than *Colman et al*., when evaluated 37 D-TGCT patients during six years. They had 13 patients with D-TGCT treated with total-arthroscopic synovectomy as the initial treatment, a second group which included eight patients that underwent anterior arthroscopic and open posterior synovectomy, and a third group where they included 16 patients treated with open anterior and open posterior surgery. They calculated the overall recurrence-free survival and observed 19% of recurrence for the open/open synovectomy group vs 25% open/arthroscopic group (eight patients) vs 92% total-arthroscopic group, concluding that the totally open synovectomy had the best recurrence free survival at two and fivw years of follow-up. [17] [18]

*Patel et al*., retrospectively analysed 114 D-TGCT during a mean of 25 months, where 102 arthroscopic or open synovectomies were performed, with a statistically higher recurrence rate in favour of the arthroscopic technique when compared with the open technique (83% vs 44%) - (p=0.0004). [19]

### b) *Osteoartrosis and need to Total Knee Arthroplasty*

During the follow-up of 80.2 months in *Akinci et al.* study, 39% needed a total knee arthroplasty (TKA) after an open synovectomy. *Jabalameli et al.* also reported history of arthrofibrosis following anterior open synovectomy in four (27%) of patients, and in two of those patients (50%) a moderate to severe osteoarthritis was identified. [12] [14]

Concerning the arthritic progression from baseline, *Colman et al*. identified a global rate of 17% - open synovectomy (0%) vs open plus arthroscopic synovectomy (9%) vs totally arthroscopic techniques (23%)- with a specific rate of 8% of patients which needed a TKA within the follow-up period, however, without statistical significant differences between groups (p=0.16). Also in *Colman et al*. study, all patients needing a TKA due to knee arthritis had a previous total arthroscopic synovectomy, but again, without no statistical significant differences comparing other patient groups.[17]

*Jitesh K et al.* mentioned in their series that no progression towards osteoarthritis was observed during the follow-up.[16] Additionally, *Vivek et al.* also did not report any data regarding arthritic progression or progression towards the need of arthroplasty, however, these authors did not reported any complications.[18]

## *Secondary Outcomes*

### a) *Articular Effusion, Pain and Limited range of motion*

*Akinci et al.* observed in three patients (20%), after open synovectomy, postoperative knee joint stiffness and none of the patients developed infection or hemarthrosis. According to the Knee Society Score (KSS): eight patients (42.2%) had perfect, nine (47.3%) had good, and two patients (10.5%) had bad clinical outcomes. [12]

In six patients with staged surgery (posterior and anterior open synovectomy), *Jabalameli et al.* reported that the KSS score improved significantly with no complications regarding knee instability. [14]

*Aurégan et al*. also reported a significant improvement in global clinical outcome after arthroscopic synovectomy, using the Tegner-Lysholm score. The improvement was from 68 (pre-operatively) to 90 points (post-operatively) - p=0.0004 - but also included cases of L-TGCT. [15]

*Patel et al*. had two cases (1%) of stiffness that required manipulation under anaesthesia (MUA) and three (2%) patients with a neurological injury and foot drop. However, the authors do not specify in which of the TGCT variants this cases were observed. Additionally, this was a single center retrospective observational study with a low mean follow up time (25 months) without report on functional outcomes. [19]

***b) Complications directly related to surgery***

*Jabalameli et al.* observed no infection or neurovascular injury in all groups studied.[14] The authors *Aurégan et al*., observed a rate of postoperative complications related with the arthroscopy procedure as low as 0%, while *Colman et al*. reported a lower postoperative complications with open posterior followed by anterior arthroscopic synovectomy.[15][17] The most common complication was hemarthrosis (6%), with no significant differences between groups.[17]

There were no complications such as infection, neurovascular damage, deep vein thrombosis or wound healing in the group studied by *Jitesh K et al.,* where total arthroscopic synovectomy were performed.[16]

*Patel et al*., in other hand, observed an overall low complication rate (9.8%). However, of this, 88.9% was due to open surgery, which included six patients with wound infection, three postoperative haemarthrosis and one case complicated with DVT.[19]

**Discussion**

The TGCT was first described by Chassaignac in 1852 and up to now remains with no consensus about the etiology and pathogenesis for this lesion, which could be considered neoplastic, inflammatory, traumatic, metabolic, and viral according to different theories. [10][20][21] New evidence suggests a clonal neoplastic origin for TGCT that include specific genetic changes, frequently associated to a specific translocation: t(1;2) CSF1:COL6A3. [6][9][22] Also, currently is being considered the *'paracrine landscape effect'* that stands for a reactive component with proliferation and recruitment of colony-stimulating factor 1 receptor (CSF1R) expressing cells that includes macrophages, giant cells and osteoclasts.[22] It should also be considered a correlation between the onset of this disease and trauma, lipometabolism and even with surgical aggression. [13]

The tenosynovial giant cell tumour frequently presents as a firm, slow-growing, multilobular, non-tender mass adjacent to the tendon sheath synovium, with similar clinical and histological features between the two different subtypes: localized and diffuse.[2] According to the 2013 WHO classification, each subgroup can be evaluated radiologically taking into account the growth pattern. Consequently, to characterize and estimate the extent of tumor growth for preoperative assessment, the MRI imaging technique is the standard method and it was the mainstay imaging study for all of the studies evaluated. [2][23]. Radiographically, the majority of these tumours present a poorly defined periarticular mass, associated with degenerative joint disease and cystic lesions in the adjacent bone. [24][25] The L-TGCT typically exhibits a conspicuous nodular form with low signal on T1WIs and T2WIs due to the presence of hemosiderin. [23] On the other hand, D-TGCT, as a villous proliferation of the synovium, results in a more heterogeneous image with larger areas of hypointensity on T1WI and T2WI. The diffuse type also presents enhanced heterogeneity on contrast-enhanced T1WI when compared with the localized form (Fig.2). [23]

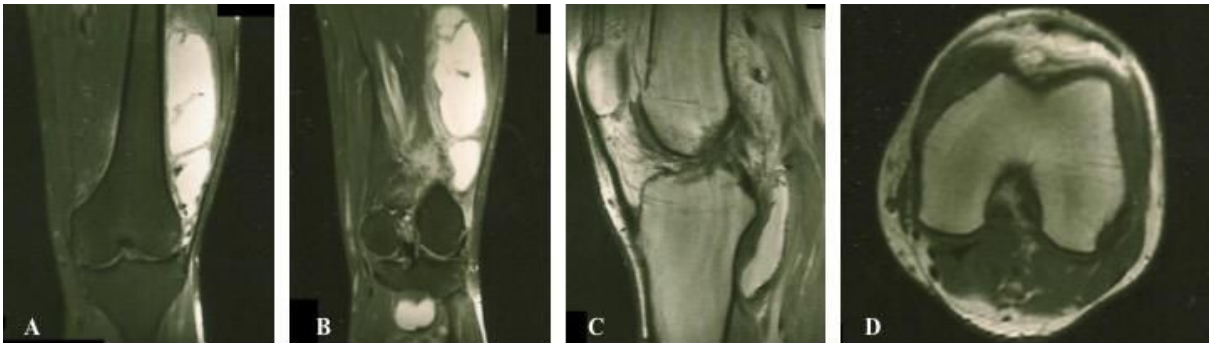


**Fig. 2.** Pre-operative MRI images of knee D-TGCT. A) T2 coronal section; B) T2 coronal section; C) T1 sagittal section; D) T1 axial section

Being a circumscribed benign small mass (usually 0.5 to 4 cm), the L-TGCT presents a more favourable course after total excision of the mass, with an overall recurrence rate relatively low: 0–6%.[6][8] Meanwhile, given the fact that D-TGCT extensively involves the synovial membrane and infiltrates adjacent structures, with a lack of clear-cut boundaries, this subtype has a much significant morbidity and impaired quality of life, even after proper treatment (Fig. 3 and Fig. 4).[8]

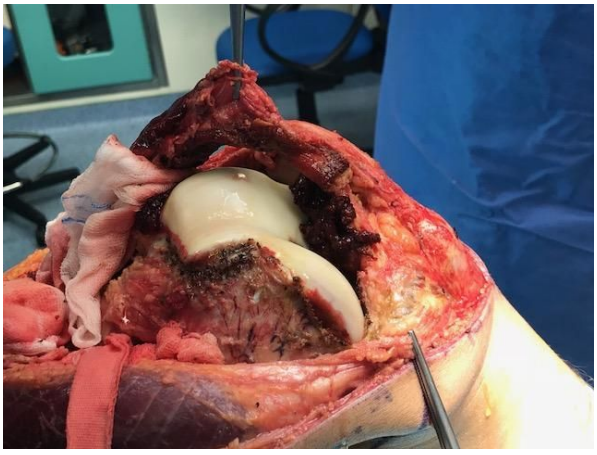

**Fig.3.** Anterior open synovectomy in diffuse tenosynovial giant cell tumor of the knee

**Fig.4.** Tumor mass after excision with anterior open synovectomy in diffuse tenosynovial giant cell tumor of the knee

A total synovectomy is the standard of care established for either L-TGCT or D-TGCT. It can be achieved with different surgical approaches as: open, arthroscopic or combined techniques with or without the complement of adjuvant therapies.[14][17] According to the literature, arthroscopic synovectomy for D-TGCT can have a local recurrence as high as 40 to 92%, while the recurrence rate it seems smaller following an open synovectomy (14%- 67%).[6][8] Nonetheless, it is not clear and consensual which surgical technique offers best general outcomes treating D-TGCT. For this reason, in this systematic review we aimed to compare the outcomes of the different surgical modalities, specifically open and arthroscopic synovectomy techniques. In this setting, we had the goal to compare the reported outcomes as discussed in the methods section, however, we should stress major limitations for this analysis, since a simple definition as for recurrence is not standard for the selected studies.

Diffuse TGCT of the knee have a high overall recurrence rate regardless of the treatment when compared to the localized variant.[17] When the extent of the disease affects the extra-articular tissue, arthroscopic synovectomy has a higher probability of being subtotal, therefore, presenting a higher relapse rate.[16][18] For this reason, *M. Jabalameli et al., Sharma et al. and K.H. Patel et* al favour open synovectomy technique when approaching diffuse TGCT.[14][18][19] Those findings are also supported by *Akinci et al*, which observed a similar low recurrence rate for open synovectomies.[12] However, this phenomena was not observed by *Guo-ping et al.*, where no statistically significant differences were found between open and arthroscopic techniques. [13] In other study, *Colman et al*. observed a significant lower recurrence rate when a staged open posterior associated with anterior arthroscopic synovectomy were performed, which in turn favours this different option to approach D-TGCT of the knee joint. [17] Despite this findings, *Auregan et al.* and *Jain et al*. both observed in non-comparative studies good recurrence rates with totally arthroscopic synovectomies.[15]

The recurrence rate in D-TGCT is mainly influenced by the residual disease due to subtotal synovectomy. [16] This non-successfull procedure usually implies subsequent surgical procedures, which are devastating to the joint, as well as to all the other surrounding structures. The sequelae can ultimately result in end-stage degenerative joint disease (DJD), which in most cases indicates the need for total joint arthroplasty, in order to relieve pain and

improve function, but at the same time with higher morbidity and impaired quality of life.[8][10]

The progression towards osteoarthritis due to the presence of the disease is difficult to measure, nonetheless, *Colman et al.* observed lower rates of arthritic progression with totally open synovectomy (0%), when compared with open plus arthroscopic synovectomy (9%), or for totally arthroscopic techniques (23%). This outcome is also important because represents an indirect measure which correlates with the need for TKA.[17][24]. Despite this assumption, in the studies herein evaluated, the rate of progression towards osteoarthritis and needing a TKA was not reported for the most of them. Only *Akinci et al*. described a rate of 37% of patients needing a TKA due to knee osteoarthritis after open synovectomy to treat D-TGCT; and *Colman et al.* observed the same phenomena for 15% of patients submitted to an arthroscopic synovectomy.[12][17] Therefore, it seems that there is no significant difference between open synovectomy and arthroscopy concerning the progression to osteoarthritis and TKA. *Jabalameli et al.* also reported two cases of osteoarthritis and one case that underwent TKA (17%) but does not specify the technique used to treat the D-TGCT in this patients.[14]

When discussing the secondary outcomes, we aimed to evaluate the presence of articular effusion, pain, limited range of motion and complications directly related with the surgical procedure itself, such as wound infection or dehiscence. *Akinci et al.* looked into the open synovectomy results and did not report any infection or hemarthrosis, however, 20% of the patients presented with postoperative knee joint stiffness. The measured KSS in the same group was bad for 10.5% of patients compared with good and perfect outcomes in 42.2% and 47.3%, respectively.[12] *Jabalamel et al.* also observed no complications in the form of knee instability, infection or neurovascular injury and showed a significant improvement in the KSS scores after surgery in patients who underwent staged open posterior and anterior arthroscopy surgery.[14]

*Aurégan et al.*, had one case of haemarthrosis after a total arthroscopic synovectomy. The overall postoperative Ogilvie-Harris score was 7.8 (which is considered good) after partial arthroscopic synovectomy and 9.3 (also considered as good) after a complete arthroscopic synovectomy.[15] Additionally, *Colman et al.,* reported an overall low perioperative

complication rate, with no significant differences between the open and arthroscopic groups.[17] For *Patel et al.*, the overall surgical complication rate was as low as 9,8%, however, 88,9% arise from open surgery. [19]

Taking all this into consideration, it is understandable that other treatment options are being explored every day. Various forms of radiation therapy (radiosynovectomy and external beam radiotherapy) have been applied in an attempt to reduce the risk of local recurrence and improve free survival as an alternative to surgery or complement. [18]. It consists in the instillation of 90-Yttrium(90Y)-labelled colloid inside the affected joint and shows positive results as adjuvant treatment after surgical synovectomy and as monotherapy in treating D-TGCT, for initial, recurrent or residual large primary disease. [14][25]. However, like any other treatment modality, radiation use is not free of complications. The potential for serious toxicity, radionecrosis, and harmful effects on bone and joint cartilage with high iatrogenic morbidity, makes it a questionable option, especially for a benign condition.[9] Therefore, novel treatment methods for TGCT are being investigated, including immunotherapy agents. [9]

Historically, conventional chemotherapy have not been proven effective in TGCT, but the finding that D-TGCT cells overexpress colony-stimulating factor 1 (CSF1), resulting in recruitment of CSF1 receptor (CSF1R)-bearing macrophages that are polyclonal and constitute the majority of the tumour, has led to considering clinical trials with CSF1R inhibitors.[6][25] These inhibitors include less potent drugs as nilotinib and imatinib, and more specific inhibitors as emactuzumab, pexidartinib or cabiralizumab. [25] Within this present era of systemic targeted and multimodality therapies in clinical trials, specifically for the diffuse and more aggressive form of TGCT, surgical resection alone may not be regarded as the gold standard in a near future.

## Conclusions

Surgical treatment methods for D-TGCT forms in the knee are complex and still controversial in the medical community given the special characteristics of this disease. In our systematic review we aimed to conclude which of the different surgical techniques (comparing between arthroscopic or open synovectomy) has better profile given the primary and secondary outcomes established in the methodology section.

Following the review herein presented we can conclude that the recurrence rate for D-TGCT is mainly dependent on a successful resection of the initial lesion, which it seems to be better obtained with open surgical techniques. Nonetheless, arthroscopic techniques showed superiority when it comes to morbidity and surgery related complications. We could not conclude about the influence of the surgical technique in progression towards osteoarthritis and need for TKA, however, a better outcome after open synovectomy seem to be the rule.

Again, we need to stress the limitations of this systematic review regarding the number and quality of articles included, which is a consequence for the rarity of this disease. The development of multicentric prospective studies regarding D-TGCT management should be promoted, in order to obtain proper answers to the questions herein presented.

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